REMARKS

Claims 14, and 18-20 are pending in this application. Claims 14, 18 and 20 were rejected under 35 U.S.C. § 112, second paragraph. Claims 14 and 20 were rejected under 35 U.S.C. § 101. Claims 14, 19 and 20 were variously rejected under 35 U.S.C. § 102(b). Claim 18 was objected to.

By this amendment, claim 18 has been amended without prejudice or disclaimer of any previously claimed subject matter. Support for the amendment to claim 18 can be found, *inter alia*, throughout the specification, for example, at page 16, lines 24-26.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

The amendments to the specification originally submitted September 6, 2002 apparently was done with incorrect page and line numbers designations. At the Examiner's request, these amendments have been re-presented herein with the correct page and line numbers.

Applicants note that the Examiner cited Barenholz et al. (U.S. Pat. No. 5,914,311) to show state of the art with respect to LDL and compositions.

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Claim Objection

Claim 18 was objected to because of an alleged informality with the use of a shorthand mutant designation. Claim 18 has herein been amended in the interest of expediting prosecution of this application. Applicants respectfully request reconsideration and withdrawal of the objection.

Rejection under 35 U.S.C. §112, second paragraph

Claims 14, 18 and 20 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection.

Applicants respectfully point out that claim 14 recites an "apo-B100 protein comprising a proteoglycan– receptor+ mutation in Site B." The apo-B100 protein contains a mutation in Site B such that the protein has a proteoglycan– receptor+ phenotype which is described in the specification as "a mutation in Site B which results in reduced LDL-proteoglycan binding activity while maintaining LDL/LDL receptor binding (proteoglycan– receptor+ mutant)" (page 8, lines 5-9). Thus, the claimed apo-B100 mutant can be identified and distinguished by this required associated phenotype.

The typographical error in claim 18 involving "position 3358 to 3359" has been corrected in the present amendment.

Applicants submit that the claims are sufficiently definite when considered in view of the specification and the understanding of those of skill in the art.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §101

Claims 14 and 20 were rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter. Applicants respectfully traverse this rejection.

As discussed above, the claimed apo-B100 protein comprises a mutation in Site B which results in a proteoglycan– receptor+ phenotype, i.e., an apo-B100 protein with reduced binding activity to proteoglycan but with normal binding activity to the LDL receptor. Thus, the claimed apo-B100 protein contains not only a sequence alteration but also an associated change in activity. Apo-B100 protein with a mutation as claimed is not known to exist in nature, nor is an LDL particle comprising such an apo-B100 protein. As such, Applicants respectfully submit that the claimed invention is directed to statutory subject matter.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 101.

Rejections under 35 U.S.C. §102(b)

Claims 14 and 19 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Law *et al.* (1990, *J. Lipid Research* 31:1109-1120, "Law"). Claims 14 and 20 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Leroy *et al.* (1992, *J. Lipid Research* 33:889-898, "Leroy"). Applicants respectfully traverse this rejection.

Law describes the amino acid sequence of a number of apo-B100 proteins from a variety of animal species. As pointed out by the Examiner, the amino acid sequence from 3359-3367 of this protein varies somewhat between the proteins of the animal species discussed in Law and the human protein. However, Applicants respectfully point out that Law does not teach an apo-B100 protein which comprises a mutation in Site B which results in proteoglycan– receptor+ activity, i.e., an apo-B100 protein with reduced binding activity to proteoglycan but with normal binding activity

to the LDL receptor. For example, the specification teaches that replacement of the lysine at position 3363 in the human apo-B100 protein with a glutamic acid residue results in the proteoglycan– receptor+ phenotype. As shown in Fig. 2 of Law, all of the apo-B100 proteins from the various species described therein have a lysine at the position 3363 equivalent. In sum, Law is silent with regard to an apo-B100 mutant protein with a proteoglycan– receptor+ activity.

Leroy describes human and rabbit apo-B100 proteins and LDL particles comprising the proteins. The Examiner points to Law as demonstrating that the sequence of the B site of rabbit apo-B100 differs from the sequence of the human apo-B100 protein. However, as with Law, Leroy is silent with regard to an apo-B100 mutant protein with a proteoglycan– receptor+ activity.

For a claim to be anticipated by a reference, the reference much teach each and every element of the claim. Neither Law nor Leroy teach an apo-B100 mutant protein with a proteoglycan– receptor+ activity. Accordingly, Applicants respectfully submit that neither Law nor Leroy anticipate the claimed invention.

Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §102(b).

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 220002059710.

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Respectfully submitted,

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